SCREENING OF COLORECTAL CANCER IN EUROPE

Which way of prevention is really feasible and useful?

Meinhard Classen

Falk Symposium
164
Intestinal Disorders
Budapest
May 2 – 3, 2008
Estimated number of CRC Cases in Europe

Eastern Europe
Czech Republic, Poland, Slovakia
112,222

Northern Europe
Denmark, Estonia, Finland, Iceland, Norway, Sweden, United Kingdom
55,315

Western Europe
Austria, France, Germany, Netherlands, Switzerland
125,008

Southern Europe
Italy, Malta, Portugal, Slovenia, Spain
79,676

Total
372,221
CRC is the 2nd most Frequent Cancer in Europe
5-year survival rate after diagnosis in Europe

White figures 1990-1994
Black figures 2000-2002

EUROSTAT 3 & 4 (Lancet Oncology 2007)
PROVEN AND NEW TESTS
CRC Screening Tests

**Stool tests**
- gFOBT
- iFOBT
- DNA
- TuM$_2$PK

**Endoscopy**
- Sigmoidoscopy
- Colonoscopy

**Radiology, MR**
- CTC
- MR
<table>
<thead>
<tr>
<th>Detection goal</th>
<th>Technology</th>
<th>Sensitivity determinants</th>
<th>Specificity determinants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal blood</td>
<td>gFOBT</td>
<td>amount of heme in feces</td>
<td>dietary heme; bleeding nonneoplastic lesions</td>
</tr>
<tr>
<td></td>
<td>iFOBT</td>
<td>amount of globin in feces</td>
<td>bleeding nonneoplastic lesions</td>
</tr>
<tr>
<td>Fecal neoplasm-derived DNA</td>
<td>Multitarget fecal DNA test</td>
<td>Spectrum of DNA changes shed into feces</td>
<td>unclear</td>
</tr>
</tbody>
</table>

Young and Allison 2007
### Guaiac-based Fecal Occult Blood Test (gFOBT)

**CRC Screening and Mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandel (1993)</td>
<td>46.551</td>
</tr>
<tr>
<td>Hardcastle (1996)</td>
<td>152.850</td>
</tr>
<tr>
<td>Kronborg (1996)</td>
<td>61.933</td>
</tr>
<tr>
<td>Kewenter (1994)</td>
<td>68.308</td>
</tr>
<tr>
<td>Faivre (2004)</td>
<td>45.642</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>375.266</strong></td>
</tr>
</tbody>
</table>

Relative Risk

- **p = 0.000**

Towel: BMJ 1998

Faivre: Gastro 2004
# Fecal Immunochemical Test (iFOBT) vs. gFOBT

<table>
<thead>
<tr>
<th>Test</th>
<th>iFOBT</th>
<th>gFOBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca Sensitivity</td>
<td>82–87%</td>
<td>54–64%</td>
</tr>
<tr>
<td>Adv. Adenoma Sensitivity</td>
<td>41–42%</td>
<td>23–30%</td>
</tr>
</tbody>
</table>

Allison et al. JNCI 2007
Smith et al. Cancer 2006
Quantitative iFOBT (OC-Micro, InSure)

Quantification of fecal hemoglobin is important!

- Hb concentration increases with pathology progressing (Ca < advanced adenoma < small adenoma)
- Pat. with advanced adenomas have higher fecal Hb concentrations than those without neoplastic path.
- Particular chosen sensitivity / specificity ratio by selection of the cut-off (independent of manufacturer)
<table>
<thead>
<tr>
<th></th>
<th>Sensitivity Colorectal Cancer (%)</th>
<th>Specificity Colorectal Cancer (%)</th>
<th>Sensitivity Advanced Adenomas (%)</th>
<th>Version</th>
</tr>
</thead>
<tbody>
<tr>
<td>*</td>
<td>65 (52-72)</td>
<td>95 (94-96)</td>
<td>20 (16-24)</td>
<td>1.0</td>
</tr>
<tr>
<td>†</td>
<td>87.5 %</td>
<td>82 %</td>
<td>-</td>
<td>1.1</td>
</tr>
</tbody>
</table>

* Aggregate of 6 studies
CRC Screening: Endoscopy

- High sensitivity for cancer and adenoma
- Inhibits cancer development by removal of adenoma prevention
- Higher direct costs
- Complications
- No RTC?
## Screening Colonoscopy Studies

<table>
<thead>
<tr>
<th></th>
<th>USA</th>
<th>NCS</th>
<th>VA</th>
<th>CONCERN</th>
<th>POLAND</th>
<th>GERMANY*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Men/Women</td>
<td>Men</td>
<td>Women</td>
<td>Men/Women</td>
<td>Men/Women</td>
<td>Men/Women</td>
</tr>
<tr>
<td>Adenomas or Cancer</td>
<td>18 %</td>
<td>37.5 %</td>
<td>21 %</td>
<td>27 %</td>
<td>22.2 % (Ca. 0.98 %)</td>
<td></td>
</tr>
<tr>
<td>Advanced Neoplasia</td>
<td>5.5 %</td>
<td>10.5 %</td>
<td>4.9 %</td>
<td>5.4 %</td>
<td>6.7 %</td>
<td></td>
</tr>
</tbody>
</table>

*3.2 Mill. Screened between 2003 and 2007

NCS – Winawer et al – Gastroenterology 2002
VA – Lieberman et al – NEJM 2000
CONCERN – Schoenfeld et al – NEJM 2005
Poland – Regula – NEMJ 2007
Germany – G. Brenner et al 2007
Screening CTC Studies

**Cotton JAMA 2004**  
OC superior to CTC

**Pickhardt NEJM 2003**  
CTC & OC Equivalent  
Polyps >8 mm

**Kim NEJM 2007**  
Resource Savings, few complications with CTC

**ACRIN Trial**  
Rigorous, multicenter,  
Large. CTC & OC Equivalent polyps >8 mm
Colorectal Cancer Screening Strategies

Population

Colonoscopy

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FOBT — iFOBT
Flex. Sig. — ↓
Stool DNA — ↑
CTC — ↑

Colonoscopy

S. Winawer 2008
## Guidelines for Colorectal Cancer Screening in Average Risk Men & Women 50 Years of Age or Older

### OPTIONS

<table>
<thead>
<tr>
<th></th>
<th>Digital rectal exam</th>
<th>FOBT*</th>
<th>Flex Sig.</th>
<th>FOBT &amp; Flex Sig.</th>
<th>DCBE</th>
<th>COLO**</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Multi Society Task Force (2008)</td>
<td>w/ endoscopy</td>
<td>Annual</td>
<td>5 yrs</td>
<td>Ann. FOBT</td>
<td>5 yrs</td>
<td>10 yrs</td>
</tr>
<tr>
<td>German S. GE (2008)</td>
<td>w/ endoscopy</td>
<td>Annual 50-55 Biannual 56-65</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10 yrs</td>
</tr>
</tbody>
</table>

USA: Further options iFOBT; DNA*
USA: CTC**
Is CRC Screening worthwhile?

- Loss of humans
- Enormous treatment costs
- Cost effectiveness of screening?
Influence of Screening on CRC Mortality

Screen detected

Nonscreen detected

Survival (%)

P<0.001

=> Earlier diagnosis increases survival!

Induced costs of patients on 5 FU/Lc eucovorin plus oxaliplatin plus Bevacizumab/Cetuximab as first line therapy

- 39,300 $
- 56,300 $
- 180,000 €

Mosaic study - Cancer 2007; 109: 1082 - 1089
CRC Screening is cost-effective!

Estimated average costs for life-year gained (threshold $50,000):

<table>
<thead>
<tr>
<th>Test</th>
<th>Cost Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOBT</td>
<td>$5691 - 17805</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>$6640 - 22012</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>$12477 - 29539</td>
</tr>
</tbody>
</table>

Assumption: Endoscopy ↓ incidence mortality 60 – 90%

References:
- Sonnenberg A et al – Am Int Med 2000; 133: 573-589
- Vigon S – Am J Med 2001; 111: 593-601
Screening of Colorectal Cancer Risk Groups

- **Sporadic (Average Risk)**
  - Age: Colonoscopy 10 years earlier than index case
  - 70 - 75%

- **Family history**
  - 15-20%

- **HNPCC**
  - 3-5%

- **FAP**
  - 1%

- **CED**
  - 1%
<table>
<thead>
<tr>
<th>High risk group</th>
<th>Life time risk of CRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary CRC</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Familial CRC</td>
<td>20%</td>
</tr>
<tr>
<td>Individuals with a personal history of CRC or colorectal adenoma</td>
<td>15 - 20%</td>
</tr>
<tr>
<td>Other diseases e.g. ulcerative colitis</td>
<td>10 - 20%</td>
</tr>
</tbody>
</table>

Vasen HF, Z Gastroenterol 2008; 46: 541-542
The Estimated Number of High Risk Individuals (CRC risk ≥ 20 %) in various EU Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>640 000</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>400 000</td>
</tr>
<tr>
<td>France</td>
<td>400 000</td>
</tr>
<tr>
<td>Italy</td>
<td>400 000</td>
</tr>
<tr>
<td>Spain</td>
<td>260 000</td>
</tr>
</tbody>
</table>
Practice Guideline:
Colorectal Cancer Screening

Review Team:
S. Winawer (Chair)
M. Classen (Co-Chair)
R. Lambert (Co-Chair)
and 15 specialists

International Consultants:
R. Smith
W. Schmiegel
D. Rex
N. Amrani
A. Zauber

Recommendations for action - implementing a program - program design - monitoring the screening program

CRC screening cascades for countries with 6 different resource levels

www.world-gastro.org/colorectal-cancer-screening.html
1. CRC second most frequent cancer in Europe
2. Results of IDCA survey among 40 GE societies in Europe available
3. gFOBT and colonoscopy are the most frequently used tools
4. New stool test and imaging procedures are emerging
5. Treatment of advanced CRC extremely costly
6. CRC screening is cost-effective
7. IDCA / WGO guideline on CRC screening assists in the decision making on national screening policy
THANK YOU FOR YOUR ATTENTION